Fluid Mechanics of Pulmonary Airway Reopening and Surfactant Molecular Behavior—An Example of Multiple Scale Interactions

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The lung consists of many bifurcating airways that terminate with alveoli, the site of gas exchange. Surfactant, a protein-phospholipid mixture, is released from alveolar type-II pneumocytes, and has the primary function of reducing the surface tension of the lining fluid. Without proper surfactant molecular function the lung is micro-mechanically unstable, leading to airway closure and insufficient gas exchange. Diseases related to inadequate surfactant function include infant respiratory distress syndrome (RDS), and possibly adult respiratory distress syndrome and asthma. To fully understand surfactant insufficiency, and thus to design optimal surfactant replacements or mechanical ventilation modalities, it is important to understand:

- the precise molecular interaction between the protein and phospholipid components. This influences the dynamic surface-tension properties of the surfactant.
- the interaction between the airway lining fluid and the dynamic surface-tension. This relationship determines the macroscale lining fluid flows within the lung, which under normal conditions stabilize the lung.
- the cellular responses to the mechanical stress required to open collapsed airways and alveoli. At an organ-level, if stresses are too large the epithelial cell membranes can be damaged and cause severe trauma to the lung.

Clearly, this system has molecular processes (protein/phospholipid interactions at the air-liquid interface) that influence macroscale phenomena (lining fluid flows, cellular responses to stress) that induce organ-level responses (atelectasis, deranged mechanical properties).

The goal of our study is to investigate surfactant transport in computational models of steady and unsteady opening of pulmonary airways to determine if physicochemical hydrodynamic interactions can be used to open pulmonary airways while minimizing mechanical stresses that might cause tissue damage. We investigate a theoretical model of the pulsatile motion of a contaminant-doped semi-infinite bubble in a rectangular channel. In this study, only a surface-inactive contaminant is studied to develop a preliminary understanding of surfactant responses during unsteady pulmonary airway reopening. Reopening is modeled as the pulsatile motion of a semi-infinite gas bubble in a horizontal channel of width $2a$ filled with a Newtonian liquid of viscosity $:$ and constant surface tension $($. A sorption model is assumed that allows for the creation and respreading of a surface multilayer. The bubble is forced *via* a time-dependent volume flux $Q(t)$ with mean and oscillatory components (Q_M and Q_T, respectively) at frequency T. The flow behavior is governed by the dimensionless parameters: $Ca_M = :Q_M/(2a($, a steady-state capillary number, which represents the ratio of viscous to surface tension forces; $Ca_S = :Q_T/(2a($, an oscillatory forcing magnitude; $S = T:a/($, a dimensionless frequency that represents the ratio of viscous relaxation to oscillatory-forcing timescales; and $A=2Ca_S/S$, a dimensionless oscillation amplitude. We find that contaminant deposition and retention in the bubble cap region occurs only at moderate frequencies if retrograde bubble motion develops during the oscillation cycle. Determination of an optimal oscillation range may be important in reducing ventilator-induced lung injury associated with infant and adult respiratory distress syndromes by increasing surfactant transport to regions of collapsed airways.

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